

I. Sequence Compliance

The Examiner states that the application fails to comply with the requirements of 37 CFR 1.821 through 1.825 with regard to sequence disclosures, citing for example the sequence listing set forth on Page 10, (“These include transition state analog peptides such as decanoyl-Arg-Lys_Arg-Arg-psi [CH₂NH]-Phe-Leu-Gly-Phe-NH₂, substrate analogs such as decanoyl-RVKR-chloromethylketone, ...”). Applicant traverses. The listing on page 10 is a prior art sequence, and is accompanied by its publication reference. Further, this sequence is not “essential material” per MPEP §608.01(p). Thus, under MPEP §2422.03, this sequence need not be set forth in a Sequence Listing. Applicant has reviewed the specification and can find no other situation where a Sequence Listing is warranted. If a Sequence Listing is warranted, Applicant will gladly comply, if the Examiner would direct the Applicant to the Sequence Listing at issue.

II. Rejections Under 35 § 112, first paragraph

Claims 40-42 are rejected under 35 U.S.C 112, first paragraph as being based on a disclosure that is not enabling. Specifically, the examiner states that the Applicants *in vitro* experiments do not enable a method of treating.

Applicant traverses. There is “nothing in the patent statute or any other statutes called to our attention which gives the Patent Office the right or the duty to require an applicant to prove that compounds or other materials which he is claiming, and which he has stated are useful for “pharmaceutical applications” are safe, effective, and reliable for use in humans.” *In re Krimmel*, 292 F.2d 948 (C.C.P.A. 1961). Indeed, even in effective treatment, one looks at relative efficacy. It is the rare case that an agent is 100 percent effective, most particularly where one is treating a disease such as AIDS.

To expedite issuance of the claims, Applicants have amended claim 40, upon which claims 41-42 depend, thereby rendering this objection moot. Applicants thank the Examiner for her suggested claim language.

Applicants believe that these amendments address the Examiner's concerns under 35 U.S.C. 112, first paragraph. Reconsideration of the rejection and withdrawal thereof is respectfully requested.

III. Rejections Under 35 § 112, second paragraph

The Examiner has rejected claims 40-42 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regards as the invention.

Regarding claim 40, the Examiner has objected to the use of abbreviations such as HIV and AAT. Applicants have attended to the Examiners instruction, and have accompanied the abbreviations with the full name of the terms that they represent thereby rendering this objection moot.

Regarding claim 40, the Examiner objects to the use of the term "AAT-like activity", as rendering the term indefinite. Applicant respectfully traverses. The Federal Circuit has held that claims will not be invalid for indefiniteness so long as "those skilled in the art would understand the scope of the claim when the claim is read in light of the specification." *North American Vaccine, Inc. v. American Cyanamid Co.*, 7 F.3d 1571, 1579 (Fed. Cir. 1993). Applicant submits that one skilled in the art would recognize that for an agent to exhibit AAT like activity, the agent would be an α_1 -antitrypsin-like agent; that is, a non-natural molecule that inhibits serine protease. Thus, a compound that is AAT like is a compound having AAT like activity, e.g. activity similar to α antitrypsin activity. See the Specification, Page 12, lines 26-27; Page 13, lines 13-14 and 19-20; Page 14, lines 24-25.

Regarding claim 40, the Examiner objects to the use of terms "host" and "treating". To expedite the allowance of claims, Applicant has amended claim 40, upon which claims 41-42 depend, thereby rendering this objection moot.

Regarding claim 40, the Examiner objects to the claim as lacking process steps and an endpoint. The Applicant thanks the Examiner for her suggested language, and have amended the claim thereby rendering this objection moot.

Regarding claim 41-42, the Examiner notes that trademark names are used in the claims. The Examiner states that these names may be used if accompanied by the full names of the compound that they represent. Applicant has amended the claim, thereby rendering this objection moot.

Regarding claims 41-42, the Examiner objects to a single inhibitor being equated with a multiplicity of inhibitors. Applicant notes that claim 40 is directed to at least one compound selected from the group consisting of HIV reverse transcriptase inhibitors and HIV protease inhibitors. Thus, the claim encompasses multiple compounds; e.g. *combinations thereof*, selected from either element of this group. This being said, Applicants note that it would be duplicative to further define either HIV reverse transcriptase inhibitors (claim 41) or HIV protease inhibitors (claim 42) as including various elements *and combinations thereof*. Applicants have amended these claims thereby rendering this objection moot.

Applicant has amended and provided new claims to more particularly point out and distinctly claim the subject matter, which Applicants regard as the invention. Applicant believes that these amendments and the remarks provided herein address the Examiner's concerns under 35 U.S.C. 112, second paragraph. Reconsideration of the rejection and withdrawal thereof is respectfully requested.

IV. Rejections Under 35 § 103

On page 6 of the Office Action, the Examiner rejected claim 40 under 35 U.S.C. 103(a) as being unpatentable over Lezdey. Applicants direct the Examiner to page 9, lines 21 to page 10, line 7 of the specification, wherein the background of the invention is described:

The anti-HIV effect of AAT as speculated by Lezdey et al., [...] was also not confirmed by actual experimental studies carried out by practitioners in the art. Two separate studies, one conducted by Anderson et al. [...];

and other by Vollenweider et al. [...], have convincingly demonstrated that naturally occurring or non-mutated AAT directed against its natural substrate, elastase, has not shown any anti-HIV activity. Similarly Harvima et al., have shown that putative tryptase receptors on T lymphocytes were not reactive with [*sic*]anti-tryptase antibody [...]. Furthermore, Meylan et al, stated that AAT natural substrates such as trypsin, factor Xa, and mast cell tryptase did not enhance the HIV infectivity[...].

Page 9 Line 21 to Page 10 Line 7.

Thus, Lezdey must be reviewed with an eye to the many references that teach away from the present invention. Further, do to the size of antitrypsin, it does not enter the cell, all activity must occur intracellularly. Only an antitrypsin like agent can actually enter the cell due to its smaller size. Lezdey neither teaches nor suggests the use of these mimics.

Applicants further submit that the focus of this inquiry must be upon whether the invention was obvious to one of ordinary skill in the art at the time the invention was made. The luxury of hindsight is not permitted.

On page 7 of the Office Action, the Examiner rejected claim 40 under 35 U.S.C. 103(a) as being unpatentable over Eisenberg. To expedite claim prosecution, Applicant has amended this claim, thereby rendering this rejection moot.

In view of the foregoing amendments and remarks, it is believed that this application is in condition for allowance. A notice to this effect is respectfully requested.

AUTHORIZATION

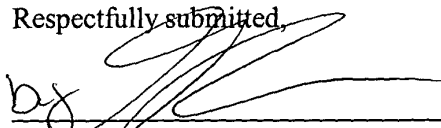
In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment to Deposit Account No. 50-1710.

CONCLUSION

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and withdraws them. There being no other objections or rejections, Applicant respectfully requests that the present application be allowed and pass to issue.

Should any further questions arise concerning this application, the Examiner is invited to call Applicants' attorney at the number listed below.

Respectfully submitted,



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APPENDIX

MARKED-UP VERSION TO SHOW CHANGES MADE

The claims are amended as follows:

40. A method for inhibiting human immunodeficiency virus (HIV) replication [treating HIV infection] in a patient [host] harboring said HIV comprising administering to the patient [the host] a therapeutically effective combination comprising: [of]
at least one first compound [of the compounds] exhibiting α_1 -antitrypsin (AAT) [AAT] or AAT-like activity, with the exception that the first compound is not serine leukocyte protease inhibitor; and
at least one second compound [one or more compounds] selected from the [a] group consisting of HIV reverse transcriptase inhibitors and HIV protease inhibitors, for a time and under conditions effective to inhibit HIV replication.
41. The method according to claim 40 wherein at least one [the] HIV reverse transcriptase inhibitor is [selected from a group consisting of Retrovir, Combivir, Eпивir, Videx, Hivid, Zerit, Ziagen, Hydrea, Viramune, Rescriptor, Sustiva, Preveon, and combination thereof] AZT/ zidovudine, 3TC, lamivudine, ddI/didanosine, ddC/zalcitabine, d4T/stavudine, abacavir, 159U89, hydroxyurea/HO, nucleoside RT potentiator, nevirapine, delavirdine, efavirenz, adefovir dipivoxil, or bis-POM PME.
42. The method according to claim 40 wherein at least one [the] HIV protease inhibitor is [selected from a group consisting of Fortovase, Norvir, Crixivan, Viracept, Angenerase, VX-478, KNI-272, CGP-61755, U-103017, and combination thereof] saquinavir, ritonavir, indinavir, nelfinavir, amprenavir, VX-478, KNI-272, CGP-61755, or U-103017.

The new claim is as follows:

46. (New) A method of inhibiting human immunodeficiency virus (HIV) replication comprising administering to a patient in need thereof, a combination of at least one

compound exhibiting α_1 -antitrypsin (AAT) or AAT-like activity and one or more compounds selected from a group consisting of HIV reverse transcriptase inhibitors and HIV protease inhibitors, for a time and under conditions effective to inhibit HIV replication.